Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 85-87 and 101 are pending in the application, with claim 85 being the independent claim. Claims 88-100 have been withdrawn from consideration. New claim 101, which depends from claim 85, is sought to be added. Support for claim 101 may be found, *inter alia*, at page 11, lines 5-8 and Examples 1 and 3 of the specification. Claims 85 and 86 have been amended to clarify the claim terms as required by the Examiner. Support for the amendments to claims 85 and 86 may be found, *inter alia*, at page 5, line 32 to page 6, line 3 and page 8, lines 27-31 of the specification. As such, these changes are believed to introduce no new matter, and their entry is respectfully requested.

Applicants respectfully request that these amendments be entered after final, as they place the claims in form for allowance.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 85-87 remain rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Office Action at pages 2-5. In particular, the Examiner alleges that the claims do not comply with the written description requirement because they encompass mutant molecules that are not disclosed in the specification. Office Action at page 3. To satisfy the written description

requirement of 35 U.S.C. § 112, first paragraph, an Applicant must convey with reasonable clarity to those skilled in the art that, as of the effective filing date, the Applicant was in possession of the invention. *See Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991).

The Federal Circuit has recently adopted the standard for determining compliance with the written description requirement as set forth in the USPTO's "Guidelines for the Examination of Patent Applications under 35 U.S.C. § 112, first paragraph, Written Description Requirement." *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1324, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002). According to the USPTO's Guidelines:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

M.P.E.P. § 2163; *See also, Enzo*, 296 F.3d at 1324, 63 USPQ2d at 1613.

Applicants respectfully assert that the specification sufficiently details the mutant molecules of the claimed methods. In particular, the specification describes and illustrates several specific mutant analogs of TNFα (*see, e.g.,* Examples 1-3) as well as methods to make and test mutant analogs for their ability to generate autoantibodies *in vivo* (*see, e.g.,* Examples 3-9). TNF-β, interleukin 1, γ-interferon and IgE are provided as further examples of self-proteins that may be used to generate other mutant analogs (*see, e.g.*, page 11, lines 5-8 of the specification). Therefore, not only does the specification teach examples of self-proteins useful in the invention and methods for

making mutant analogs of these self-proteins, but also discloses methods to test the mutant analogs for the asserted activity.

Moreover, Applicants are not required to disclose or provide a working example of every species of a given group in order to meet the written description requirement of 35 U.S.C. § 112. *See Ex parte Parks*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. Int. 1994), *In re Alton*, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996). As such, Applicants respectfully assert that in view of the above-noted disclosure, the claims as amended do satisfy the written description requirement. Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 85-87 remain rejected under 35 U.S.C. § 112 as allegedly indefinite. Office Action at pages 5-9. In particular, the Examiner emphasizes that Attorney arguments cannot take the place of evidence of record. Office Action at page 7. Applicants respectfully traverse the rejection as may apply to the claims as amended.

Claim 85 is rejected because the phrase "the tertiary structure of the pathogenic self-protein is essentially preserved" is allegedly unclear. Office Action at page 5. Not in acquiescence to the propriety of the rejection, but rather solely to advance prosecution, Applicants have amended claim 85 to specify that the analog "induces an antibody response as evidenced by antibody binding to the unmodified self-protein," as suggested by the Examiner (*see, e.g.*, page 5, line 32 to page 6, line 3 and page 8, lines 27-31 of the specification). Accordingly, Applicants respectfully assert that amended claim 85 is definite, and respectfully request that the rejection be reconsidered and withdrawn.

Claim 86 is rejected because the phrase "preserve flanking regions" is allegedly unclear. Office Action at page 8. Not in acquiescence to the propriety of the rejection, but rather solely to advance prosecution, Applicants have amended claim 86 to specify that the foreign T-cell epitope is inserted so as to preserve the "amino acid sequences from the original pathogenic self-protein on both sides of the T-cell epitope." As such, Applicants respectfully assert that amended claim 86 is definite, and respectfully request that the rejection be reconsidered and withdrawn.

Claim 85 is also rejected because the phrase "pathogenic self-protein" is allegedly unclear. Office Action at page 8. The specification describes a self-protein as a protein that causes or is capable of causing disease. *See, e.g.*, page 1, line 30 to page 2, line 2 of the specification. Every nuance of the claims does not have to be explicitly described in the specification. *See, e.g., Vas-Cath, Inc. v Mahurkar*, 935 F.2d 1555 at 1563 (Fed. Cir. 1991); *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating "the description need not be in *ipsis verbis* [*i.e.*, "in the same words"] to be sufficient"). M.P.E.P. § 2163. In view of the disclosure in the present specification, Applicants assert that the phrase "pathogenic self-protein" is definite. Applicants have also added claim 101, which specifies that the pathogenic self-protein is selected from the group consisting of TNFα, TNFβ, interleukin 1, γ-interferon and IgE. Accordingly, Applicants respectfully request that the rejection, as it may apply to the amended claims, be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 102

Claims 85 and 86 remain rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Russell-Jones *et al.* (WO 92/05192), as evidenced by Dean *et al.* (U.S. Pat. No. 5,716,596). Office Action at pages 9-12. In particular, the Examiner emphasizes that Attorney arguments cannot take the place of evidence of record. Office Action at page 11. Applicants respectfully traverse the rejection as it may apply to the claims as amended.

In regard to the Examiner's comments about the evidence of record, Applicants respectfully remind the Examiner that such evidence is available to support Applicants' arguments. *See, e.g.*, the Declarations submitted on October 9, 2000 and May 23, 2002. In particular, Applicants note the Declarations of Dr. Travers and Dr. Zinkernagel which conclude that Russell-Jones does not lead or enable one of ordinary skill in the art to arrive at the present invention. *See, e.g.*, paragraph 10 of Dr. Travers' Second Declaration, asserting that the Examiner's application of Russell-Jones strains the term "immunogen" well beyond its well-known, ordinary, and art-accepted definition.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987); *see also* M.P.E.P. § 2131. The Examiner asserts that Russell-Jones teaches that, through the use of recombinant DNA technology, the TraT peptide can be inserted into an immunogen via substituting the TraT peptide for a peptide contained in the immunogen. Office Action at page 9. However, closer inspection of the cited passages by the Examiner

(pages 31-32) reveals that Russell-Jones does not disclose an analog of a *self-protein*, but rather replacement of so called "suppressor regions" in "otherwise immunogenic molecules" such as HIV gp120. The use of "otherwise immunogenic proteins" in Russell-Jones is also supported by the disclosure on page 8, line 36 through page 9, line 3 which states, in relevant part, "[T]ypically, the at least one "immunogen" will be a molecule which is poorly immunogenic, but immunogenic molecules are not excluded." The claimed invention is directed to substituting existing regions of self-proteins so that an immune response is generated because the original, self-proteins are not immunogenic at all.

In addition, contrary to the assertion by the Examiner, somatostatin is not a pathogenic self-protein. As evidenced by Dean, somatostatin is a tetradecapeptide which, in native configuration, is of limited use. (Dean, col. 1, lines 20-41). Also, as a tetradecapeptide, one could not substitute one or more fragments of somatostatin with a foreign T cell epitope such that the structure of the protein is essentially preserved.

Therefore, since Russell-Jones, even as evidence by Dean, does not disclose substitutions of self-proteins such that the tertiary structure is essentially preserved, it does not teach each and every element of the claims as amended. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 103

Claims 85-87 remain rejected under 35 U.S.C. § 103 as allegedly unpatentable over Russell-Jones (of record) in view of Dean (of record). Office Action at pages 12-15. In particular, the Examiner emphasizes that Attorney arguments cannot take the

place of evidence of record. Office Action at page 14. Applicants respectfully traverse the rejection as it may apply to the claims as amended.

In regard to the Examiner's comments about the evidence of record, Applicants respectfully remind the Examiner that such evidence is available to support Applicants' arguments. *See, e.g.*, the Declarations submitted on October 9, 2000 and May 23, 2002. As mentioned above, the Declarations of Dr. Travers and Dr. Zinkernagel conclude that Russell-Jones does not lead or enable one of ordinary skill in the art to arrive at the present invention. Also, Applicants remind the Examiner of the Declarations of Mr. Schmidt and Mr. Borregaard which provide additional evidence of the technical, commercial and financial success of the invention sufficient to rebut a *prima facie* case of obviousness. *See, e.g.*, the Declarations submitted on October 9, 2000 and May 23, 2002.

In order to establish a *prima facie* case of obviousness, the proper analysis is to first consider whether the following three criteria are met: (1) there must be some reason, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. M.P.E.P. § 2143. "[I]n formulating a rejection under 35 U.S.C. § 103(a) based upon a combination of prior art elements, it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed." Memorandum from the United Patent and Trademark Office, "Supreme Court decision on *KSR Int'l. Co. v. Teleflex Inc.*," (May 3, 2007) at page 2. Applicants respectfully

assert that the Examiner has not provided an adequate reason to combine the reference teachings and arrive at Applicants' claimed invention, and thus the first criteria necessary to establish a *prima facie* case of obviousness has not been met.

As mentioned above, Russell-Jones describes the identification of T cell epitopes from the TraT protein and further their use in enhancing immune responses to immunogens. Russell-Jones does not disclose generation of an analog of a *self-protein*, but at best, replacement of so called "suppressor regions" in "otherwise immunogenic molecules" such as HIV gp120. The deficiencies of Russell-Jones are not cured by Dean. Dean discloses *radiolabeled* somatostatin-derived peptides and their use in imaging and therapy.

As amended, the claims are directed to administering an analog of a self-protein made by molecular biological means, to induce autoantibodies in a subject. Applicants respectfully assert that there is no reason in Russell-Jones, Dean or the general knowledge in the art to combine these references. As mentioned above, since somatostatin is a tetradecapeptide, it cannot be used to make an analog that would retain the necessary tertiary structure to induce autoantibodies. Therefore, rather than support the Examiner's argument, Dean actually teaches away from the combination of references. A prior art reference must be considered in its entirety, including portions that would lead away from the claimed invention. *See* M.P.E.P. § 2141.02(VI) (citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983)); *see also Panduit Corp. v. Dennison Mfg. Co.*, 774 F.2d 1082, 1093-94 (Fed. Cir. 1985) ("The well established rule of law is that each prior art reference must be evaluated as an entirety . . . ."). That is, "[t]here is no suggestion to combine . . . if a reference teaches

away from its combination with another source." *Tec Air, Inc. v. Denso Manufacturing Michigan Inc.*, 192 F.3d 1353, 1360 (Fed. Cir. 1999); *see also KSR* at 12 (reaffirming "the corollary principle that when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious") (citing *United States v. Adams*, 383 U.S. 39, 51-52 (1966)). At best, Russell-Jones is an invitation to manipulate otherwise immunogenic molecules, and not to manipulate a self-protein, *which is non-immunogenic,* to cause production of autoantibodies when administered to a subject. As such, Russell-Jones in view of Dean does not render the claims as amended obvious. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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